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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,266	12/20/2006	Sabine Gack	085449-0188	3606

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FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
10/08/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,266	GACK ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *29-64* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed on 12/20/2008, is acknowledged.

2. Claims 29-64 are pending and being acted upon presently.

Election/Restrictions

3. Restriction is required under 35 U.S.C. 121 and 372.
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

4. In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

I. Claims 29-31, drawn to a method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising determining the expression level of a peptide or polypeptide ADAM-12.

II. Claims 35-37, 45, drawn to a method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising measuring the amount of a ligand bound to a peptide or polypeptide ADAM-12, wherein the ligand is **KB-R7785** or derivative thereof.

III. Claims 35-37, 45, drawn to a method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising measuring the amount of a ligand bound to a peptide or polypeptide ADAM-12, wherein the ligand is **TIMP-1**.

IV. Claims 35-37, 45, drawn to a method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising measuring the amount of a ligand bound to a peptide or polypeptide ADAM-12, wherein the ligand is **TIMP-2**.

V. Claims 35-37, 45, drawn to a method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and

gestational diabetes, comprising measuring the amount of a ligand bound to a peptide or polypeptide ADAM-12, wherein the ligand is **TIMP-3**.

VI. Claims 35-37, 45, drawn to a method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising measuring the amount of a ligand bound to a peptide or polypeptide ADAM-12, wherein the ligand is **IGFBP-5**.

VII. Claims 35-37, 45, drawn to a method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising measuring the amount of a ligand bound to a peptide or polypeptide ADAM-12, wherein the ligand is **PKC-δ**.

VIII. Claims 35-37, 45, drawn to a method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising measuring the amount of a ligand bound to a peptide or polypeptide ADAM-12, wherein the ligand is **α-actinin**.

IX. Claims 35-37, 45, drawn to a method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising measuring the amount of a ligand bound to a peptide or polypeptide ADAM-12, wherein the ligand is **α-actinin-2**.

X. Claims 35-37, 45, drawn to a method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising measuring the amount of a ligand bound to a peptide or polypeptide ADAM-12, wherein the ligand is **src**.

XI. Claims 35-37, 45, drawn to a method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising measuring the amount of a ligand bound to a peptide or polypeptide ADAM-12, wherein the ligand is **Grb-2**.

XII. Claims 35-37, 45, drawn to a method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising measuring the amount of a ligand bound to a peptide or polypeptide ADAM-12, wherein the ligand is **syndecan-4**.

XIII. Claims 35-37, 45, drawn to a method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising measuring the amount of a ligand bound to a peptide or polypeptide ADAM-12, wherein the ligand is **antibodies**.

XIV. Claims 35-37, 45, drawn to a method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising measuring the amount of a ligand bound to a peptide or polypeptide ADAM-12, wherein the ligand is **nucleic acid aptamers**.

XV. Claims 35-37, 45, drawn to a method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising measuring the amount of a ligand bound to a peptide or polypeptide ADAM-12, wherein the ligand is **protein aptamers**.

XVI. Claims 38-43, 45, drawn to a method for the diagnosis of a disease selected from the group consisting of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, and gestational diabetes, comprising determining the expression level of a nucleic acid molecule of ADAM-12 (SEQ ID NO: 1 or 3).

XVII. Claim 44, drawn to a method for the identification of ligands binding specifically to a peptide or polypeptide of SEQ ID NO: 2 or 4 encoded by a nucleic acid of SEQ ID NO: 1 or 3, comprising the following steps: a) contacting the polypeptide with at least one candidate for a ligand; b) measuring the binding of the candidate for a ligand to the polypeptide.

XVIII. Claims 46-53, drawn to a diagnostic composition or a kit comprising a specifically binding ligand that specifically binds to a peptide or polypeptide of SEQ ID NO: 2 or 4.

XIX. Claims 46-53, drawn to a diagnostic composition or a kit comprising a nucleic acid molecule of SEQ 1D NO: 1 or 3.

XX. Claims 54-56, drawn to a method for the treatment of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, or gestational diabetes, comprising administering to a patient in need thereof a therapeutically effective amount of a nucleic acid molecule comprising SEQ ID NO: 1 or 3.

XXI. Claim 59, drawn to a method for the treatment of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, or gestational diabetes, comprising administering to a patient in need thereof a therapeutically effective amount of an inhibitor of the biological activity of a peptide or polypeptide with a sequence presented in SEQ ID No. 2 or 4, wherein the inhibitor is **KB-R7785**.

XXII. Claim 59, drawn to a method for the treatment of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, or gestational diabetes, comprising administering to a patient in need thereof a therapeutically effective amount of an inhibitor of the biological activity of a peptide or polypeptide with a sequence presented in SEQ ID No. 2 or 4, wherein the inhibitor is **A TIMP**.

XXIII. Claim 59, drawn to a method for the treatment of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, or gestational diabetes, comprising administering to a patient in need thereof a therapeutically effective amount of an inhibitor of the biological activity of a peptide or polypeptide with a sequence presented in SEQ ID No. 2 or 4, wherein the inhibitor is **TIMP-3 or a fragment thereof**.

XXIV. Claim 59, drawn to a method for the treatment of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, or gestational diabetes, comprising administering to a patient in need thereof a therapeutically effective amount of an inhibitor of the biological activity of a peptide or polypeptide with a sequence presented in SEQ ID No. 2 or 4, wherein the inhibitor is **α2-Macroglobulin**.

XXV. Claim 59, drawn to a method for the treatment of preeclampsia, eclampsia, pregnancy induced hypertension, HELLP syndrome, intrauterine growth retardation, superimposed gestosis, or gestational diabetes, comprising administering to a patient in need thereof a therapeutically effective amount of an inhibitor of the biological activity of a peptide or polypeptide with a sequence presented in SEQ ID No. 2 or 4, wherein the inhibitor is **an antibody directed against ADAM 12**.

XXVI. Claims 62-63, drawn to a method for identification of an inhibitor of the biological activity of a peptide or polypeptide of ADAM 12, comprising the following steps: contacting said peptide or polypeptide with a suitable substrate, e.g. HB-EGF.

XXVII. Claim 64, drawn to a method for the preparation of a pharmaceutical composition comprising the identified inhibitor.

Claims 32-34 link inventions II-XV. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claims, claims 32-34.

Claims 57-58 and 60-61 link inventions XXI-XXV. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claims, claims 57-58 and 60-61.

Upon the allowance of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claims will be entitled to examination in the instant application. Applicants are advised that if any such claims depending from or including all the limitations of the allowable linking claims are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

5. The inventions listed as Groups I-XXVII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The invention of Groups XVIII and XIX were found to have no special technical feature that defined the contribution over the prior art of Gilpin et al (IDS reference) (see entire document).

Gilpin et al teach polyclonal and monoclonal (such as 14E3) antibodies against ADAM 12 that would specifically bind to a polypeptide of SEQ ID NO: 2 or 4. Gilpin teaches that hybridomas were grown in DMEM (see page 158, under *Purification of recombinant ADAM 12 and Production of Poly- and Monoclonal Antibodies* in particular). Gilpin et al further teaches sense primer at nt 3252-3274 of ADAM 12-S and antisense primer at nt 2498-2474 of ADAM 12-L. Also Gilpin et al teaches the nucleotide probes used to hybridized to the ADAM 12 pro-domain (nt664-1007), disintegrin domain (nt4227-5067) of ADAM 12-L (see page 158, under *Analysis of Alternatively spliced Exons* in particular).

Since Applicant's inventions do not contribute a special technical feature when viewed over the prior art they do not have a single general inventive concept and so lack unity of invention.

5. **Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined** even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention.**

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.
If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.
Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Species Election

7. Irrespective of whichever group applicant may elect, applicant is further required under 35 US 121 (1) to elect a single disclosed species to which claims would be restricted if no generic claim is finally held to be allowable and (2) to list all claims readable thereon including those subsequently added.

A. If any one Groups I-XVI or XVII-XIX is elected, applicant is required to elect a single specific mean or agent for the measurement of expression of the (a) genes or b) proteins, c) blood pressure d) a specific combination, wherein the genes or proteins is one of the genes or proteins recited in claims 31, 36, 42 or 47. These are distinct species because their structures and modes of action are different which, in turn, address different therapeutic endpoints.

B. If any one of Groups I-XVI or XX-XXV is elected, applicant is required to elect a particular disease to be diagnosed/treated such as a) preeclampsia, b) eclampsia, c) pregnancy induced hypertension, d) HELLP syndrome, e) intrauterine growth retardation, f) superimposed gestosis or g) gestation diabetes. These species are distinct because the pathological conditions differ in etiologies and therapeutic endpoints; thus each condition represents patentably distinct subject matter.

8. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species;

and/or the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected species,** including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election of the species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

9. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double

patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

10. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B. O'Hara can be reached on (571) 272-0878. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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/Maher M. Haddad/
Maher Haddad, Ph.D.
Primary Patent Examiner
Technology Center 1600